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Stereoselective acid-catalyzed homoallylic rearrangement of cyclopropylsilylmethanols: an efficient route to *Z*-homoallyl derivatives

Mitsunori Honda,* Yuichi Yamamoto, Hideki Tsuchida, Masahito Segi and Tadashi Nakajima

Division of Material Sciences, Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa, Ishikawa 920-1192, Japan

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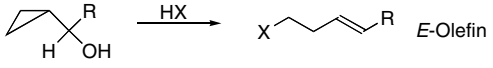
Abstract—Treatment of cyclopropylsilylmethanols derived from cyclopropyl silyl ketones with acid catalyst gives the corresponding silyl-substituted homoallyl derivatives in high yields with good stereoselectivity, independent of the substituents on the cyclopropyl ring. Cyclopropylsilylmethanols having a *n*-, *s*-butyl or phenyl group on the carbinyl carbon react to afford the *E*-homoallyl derivatives selectively. On the other hand, the reaction of cyclopropylsilylmethanols having a *tert*-butyl group gives *Z*-isomers exclusively. The following protiodesilylation of the resulting homoallyl derivatives proceeds with retention of configuration.

Acylsilanes have received considerable attention due to their unusual spectroscopic properties, novel chemical reactivity, and their utility as useful synthons in organic synthesis.[1] Especially, cyclopropyl silyl ketones[2,3] are expected to exhibit the specific reactivities of the three-membered ring[4] and the silylcarbonyl group. Nevertheless, it is relatively difficult to synthesize them. Thus, only a few reports have been published for the synthesis of them.[2] On the other hand, we have already reported facile synthetic method of cyclopropyl silyl ketones[2c] by the reaction of 1-lithio-1-trimethylsilylcyclopropanes with dichloromethyl methyl ether and presented the synthetic utilization of them.[3] In this paper, we describe the nucleophilic addition reaction[5–7] to the carbonyl group of the cyclopropyl silyl ketones and the subsequent acid-catalyzed homoallylic rearrangement of the resulting silylmethanols for the formation of silyl-substituted homoallyl derivatives.

In general, homoallylic rearrangement of the cyclopropylmethanol is known as the Julia olefin synthesis[8–10] that leads to the stereoselective formation of the *E*-homoallyl derivatives (Scheme 1). We considered that a bulky silyl group acts as a directing group for stereoselectivity on this olefin synthesis. The strategy for the synthesis of *Z*-homoallyl derivatives is as follows. The homoallylic rearrangement of cyclopropylsilylmethanols derived from cyclopropyl silyl ketones is expected to lead to the stereoselective formation of *E*-silyl-substituted homoallyl derivatives, and the following protiodesilylation[11] should proceed with retention of configuration. Thus, it can be seen that the geometry of the alkene moiety of protiodesilylated products is the opposite to that of Julia reaction using the corresponding cyclopropylmethanols (Scheme 2). Incidentally, homoallylic rearrangement of the cyclopropylsilylmethanols derived from the reduction of cyclopropyl silyl ketones has been reported by Ohfune and co-workers.[10] However, stereochemistry of the reaction using tertiary silylmethanol has not yet been studied.



Scheme 1. Julia olefin synthesis.

The nucleophilic addition reaction with organolithium reagents to cyclopropyl silyl ketones was examined

Keywords: Acylsilanes; Nucleophilic addition; Cyclopropylmethanol; Homoallylic rearrangement; Protiodesilylation.
* Corresponding author. Tel.: +81 76 234 4789; fax: +81 76 234 4800; e-mail: honda@t.kanazawa-u.ac.jp

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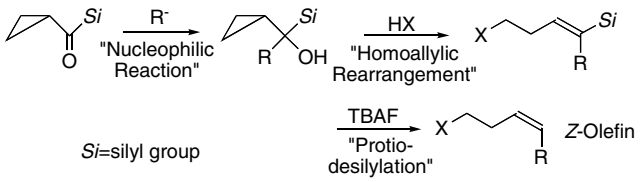
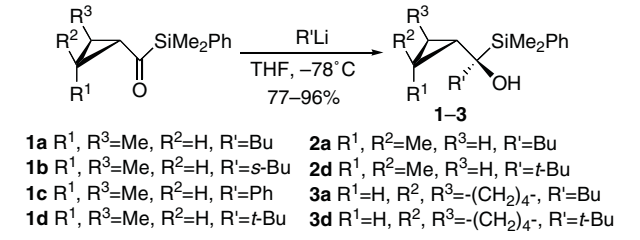
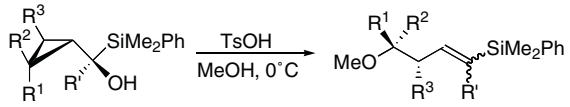


Scheme 2.



Scheme 3. The nucleophilic addition reaction with organolithium reagents.

Table 1. TsOH catalyzed homoallylic rearrangement of cyclopropylsilylmethanols



Entry	Substrate	R^1	R^2	R^3	R′	Product	Yield (%)[a]	E/Z[b]
1	**1a**	Me	H	Me	Bu	**4a**	86	>99/1
2	**1b**				*s*-Bu	**4b**	72	>99/1
3	**1c**				Ph	**4c**	52	>99/1
4	**1d**				*t*-Bu	**4d**	90	1/>99
5	**2a**	Me	Me	H	Bu	**5a**	68	>99/1
6	**2d**				*t*-Bu	**5d**	70	1/>99
7	**3a**	H	$-(CH_2)_4-$		Bu	**6a**	74	>99/1
8	**3d**				*t*-Bu	**6d**	72	1/>99

Molar ratio; cyclopropylsilylmethanol/TsOH/MeOH = 1:3:40.
[a] Isolated yield.
[b] Determined by ^{1}H NMR analysis.

(Scheme 3).[7] Acylsilanes were treated with alkyllithium or phenyllithium at −78 °C in THF. The reaction proceeded smoothly to afford the corresponding silyl alcohols **1**–**3** in high yields. It was found that the reaction of 2,3- or 2,2-dimethylcyclopropyl dimethylphenylsilyl ketone with alkyllithium reagents provided only one isomer as shown in Scheme 3 among the two possible diastereomeric products.[6]

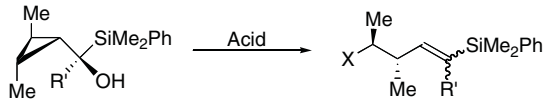
Then, treatment of cyclopropylsilylmethanols derived from the above reaction with TsOH in methanol was carried out.[12] The homoallylic rearrangement proceeded to give silyl-substituted homoallyl ethers stereoselectively. The results are summarized in Table 1. In a typical experiment to produce exclusively homoallyl ethers, cyclopropylsilylmethanol solution (0.5 mmol in 0.8 ml of methanol) was placed in a round-bottomed flask under argon, followed by the addition of TsOH (1.5 mmol) at 0 °C. The mixture was stirred for 0.5 h. The reaction mixture was quenched with a sodium hydrogen carbonate aqueous solution. The product was extracted with pentane, washed with brine, dried with anhydrous Na_2SO_4, concentrated under reduced pressure, and separated with silica gel chromatography using a mixture of hexane and dichloromethane as the eluent, affording the corresponding homoallyl ethers.

The yields in homoallyl derivatives were generally reasonable, irrespective of the substituents on the cyclopropyl ring or the carbinyl carbon. The reaction of cyclopropylsilylmethanols having a *n*-, *s*-butyl or phenyl group on the carbinyl carbon afforded the *E*-isomer selectively (entries 1, 2, 3, 5, and 7). On the other hand, cyclopropylsilylmethanols having a *tert*-butyl group on the carbinyl carbon reacted to yield the corresponding *Z*-isomer with high stereoselectivity (entries 4, 6, and 8). It should be noted that the epimerization was not observed in this rearrangement reaction.

The reaction was tested with another acid catalyst. The results are summarized in Table 2. The reaction using acetic acid also proceeded smoothly to give the corresponding acetoxy compounds as mentioned above except for high reaction temperature (entries 1 and 2). Additionally, by using boron trifluoride diethyl etherate as Lewis acid in dichloromethane, the reaction progressed to give the corresponding homoallyl alcohols (entries 3 and 4).[13] Noteworthy, this reaction proceeded with catalytic amounts of boron trifluoride diethyl etherate. The homoallyl alcohols were produced by attack of hydroxy group abstracted from starting alcohols by boron trifluoride diethyl etherate in these reactions. Similarly, treatment of silylmethanols with hydrobromic acid or sulfuric acid gave the corresponding products (entries 5 and 6).

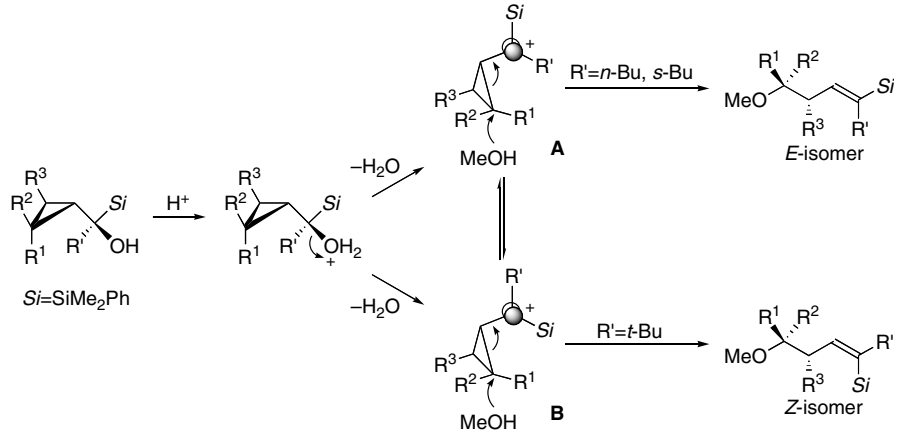
These results suggest that the stereochemistry of homoallylic rearrangement of the cyclopropylsilylmethanols is dependent on the steric repulsion between substituents on the carbinyl carbon and the three-membered ring. Thus, the following mechanism for the reaction is proposed (Scheme 4). The acid protonates at the oxygen atom of starting alcohol and bisected cation species[8a,10,14] **A** and **B** are formed. When *Si* group is larger than R′ (*n*- or *s*-alkyl), formation of bisected cation **A** is favored compared to **B** due to the less strain between R′ group and the three-membered ring. Thus, *E*-silylalkene is formed selectively. Since the attack of methanol to cation intermediate **A** proceeds in an S_N2' manner, no epimerization is observed at all. Especially, in the reaction of cyclopropylsilylmethanols **2a** and **2d** having a 2,2-dimethylcyclopropyl group, regioselective attack of methanol occurs at more substituted carbon because the positive charge would be more located at that carbon as ring-opening proceeds. In contrast, in the case of the reaction using cyclopropylsilylmethanols having a *tert*-butyl group on the carbinyl carbon, bisected cation **A** is disfavored by the steric repulsion between *tert*-butyl group, that is, bulky compared with dimethylphenylsilyl group and cyclopropyl group. Although the *Si* group is also bulky, the long Si–C single bond reduces the effective steric hindrance.[15] As a result, the reaction

Table 2. The effect of acids in homoallylic rearrangement



Entry	Substrate	R′	Acid	Solvent	Temp (°C)	Product	X	Yield (%)[a]	*E*/*Z*[b]
1	**1a**	Bu	AcOH[c]	—	110	**7a**	OAc	86	>99/1
2	**1d**	*t*-Bu	AcOH[c]	—	110	**7d**	OAc	65	1/>99
3	**1a**	Bu	$BF_3{\cdot}OEt_2$[d]	CH_2Cl_2	0	**8a**	OH	75	>99/1
4	**1d**	*t*-Bu	$BF_3{\cdot}OEt_2$[d]	CH_2Cl_2	0	**8d**	OH	70	1/>99
5	**1a**	Bu	HBr[e]	THF	0	**9a**	Br	65	>99/1
6	**1a**	Bu	H_2SO_4[e]	THF/H_2O	0	**8a**	OH	50	>99/1

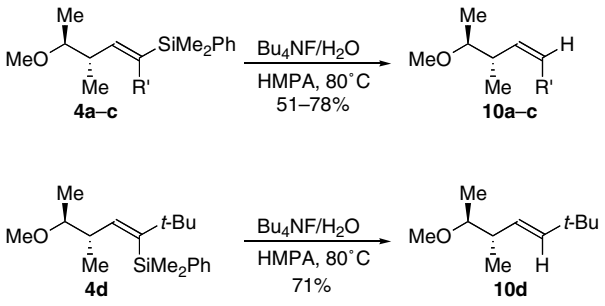
[a] Isolated yield.
[b] Determined by ^1H NMR analysis.
[c] Molar ratio; **1**/AcOH = 1:100.
[d] Molar ratio; **1**/$BF_3{\cdot}OEt_2$/solvent = 1:0.1:40.
[e] Molar ratio; **1**/acid/solvent = 1:3:40.



Scheme 4. Mechanism of the homoallylic rearrangement of silyl-substituted cyclopropylmethanol.

leads to *Z*-silylalkene with high stereoselectivity by way of bisected cation **B**.

The protiodesilylation of vinylsilane proceeds with complete retention of the configuration.[11] Thus, protiodesilylation of resulting *E*- and *Z*-silyl-substituted homoallyl derivatives **4** was examined and the results are shown in Scheme 5. Treatment of *E*- and *Z*-**4** with tetrabutylammonium fluoride (TBAF) in hexamethylphosphoric triamide at 80 °C for 1 h gave the corresponding *Z*- and *E*-protiodesilylated compounds **10**, respectively.



Scheme 5. Protiodesilylation of homoallyl ethers **4**.

In conclusion, acid-catalyzed homoallylic rearrangement of cyclopropylsilylmethanols has been described. Cyclopropylsilylmethanols reacted with TsOH in methanol to afford the corresponding homoallyl ethers in high yields with good stereoselectivity, irrespective of the substituents on the cyclopropyl ring. Cyclopropylsilylmethanols having a *n*-, *s*-butyl or phenyl group on the carbinyl carbon reacted to afford the *E*-homoallyl ethers selectively. On the other hand, the reaction of cyclopropylsilylmethanols having a *tert*-butyl group gave *Z*-isomers exclusively. The following protiodesilylation of the resulting homoallyl ethers proceeded with retention of configuration. Thus, it was achieved that the geometry of the alkene moiety of protiodesilylated products is the opposite to that of the Julia reaction using the corresponding cyclopropylmethanols. Further applications of the resulting silyl-substituted homoallyl ethers are now in progress in our laboratory. The results will be reported in due course.

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